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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/821,906	04/09/2004	David H. B. Ripin	PC25498A	2445
23913	7590	08/11/2005	EXAMINER	
PFIZER INC 150 EAST 42ND STREET 5TH FLOOR - STOP 49 NEW YORK, NY 10017-5612			TRUONG, TAMTHOM NGO	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 08/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/821,906

Applicant(s)

RIPIN ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7-5-05 (Election)
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
4a) Of the above claim(s) 2 and 30-40 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1 and 3-29 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 8/9/04 & 1/24/05
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

DETAILED ACTION

It is acknowledged that applicant has elected with traverse Group I (claims 1, 3-14 (in part) and 15-29) in the reply of 7-5-05. The traversal is on the ground that "it is improper and an abuse of discretion because prosecution of the restricted subject matter in one application would not place a serious burden on the Examiner." Said traversal is not found persuasive for the following reasons:

- a. The processes of Groups I and II have different sequence of reaction steps. Thus, a reference reading on the process of Group I would not do so to group II.
- b. The processes of Groups III and IV are drawn to the two different methods of preparing an intermediate of formula 3a. Thus, a reference reading on Group I or II would not do so to Group III or IV, and vice versa.
- c. Thus, not only there is a serious burden of searching all four groups, there is also a burden in examining each process.

Therefore, the restriction requirement is deemed proper, not "an abuse of discretion", and thus, made FINAL.

Claims 2 and 30-40 are withdrawn from consideration as being drawn to the non-elected subject matter.

Pending claims are 1 and 3-29.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1, 3-24, and 26-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 recites the definition of R^{12} which includes moieties such as: -

$NR^7C(O)NR^8R^9$, and $-NR^7SO_2NR^8R^9$. It is not clear if R^7 and R^9 in those moieties can also form a ring since " R^7 and R^9 ,..., when attached to a nitrogen atom, can be taken

together to form a 4 to 10 membered heterocyclic ring..." Note, it seems that R^7 and R^9 are not required to be attached to the **same** nitrogen atom in order to form a ring.

Because it is not clear what is intended for R^7 and R^9 in said moieties, the scope of R^{12} has indefinite metes and bounds, which renders claim 1 indefinite.

b. Claim 19 recites the phrase "wherein the base is wherein said base is" which is a typographical error. The claim also recites the limitation of " Q is ... $(R)_4N$,..." which needs a (+) charge because it is a quaternary ammonium.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

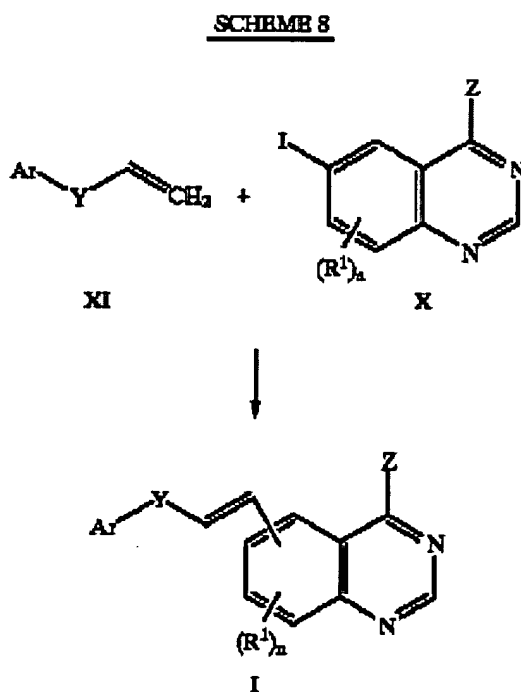
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skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 1, 3-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Sobolov-Jaynes et. al.** (US 6,225,318 – different inventive entity but commonly assigned) in view of **Berrée et. al.** (Syn. Comm., 29(15), 2685-2693 (1999)). On columns 13 and 14, Sobolov-Jaynes discloses a generic reaction of Scheme 8 in which the vinyl side chain (i.e., $-\text{CH}_2=\text{CH}-\text{Y}-\text{Ar}$) is added to the benzo ring of the quinazoline moiety, see below:



Note, the variables in formula X are defined as followed:

Z is $-NR^3R^4$, wherein

R^3 is hydrogen and R^4 can be phenyl substituted with $(R^5)_q$;

R^5 can be alkoxy, phenoxy, benzyloxy, which is equivalent to the instant –
 OR^3 ;

Thus, Z is equivalent to the instant $R^1N\text{-Phenyl}(OR^3)(R^{11})_p$.

R^1 represents many moieties that are within the scope of the instant R^6 .

So, the disclosed formula X corresponds to the instant formula 2. Likewise, the disclosed formula XI is analogous to the instant formula 3 when its variables have the following meanings:

Y is $(CH_2)_p$ wherein p is 0-5 and wherein one or two of the CH_2 groups may optionally and independently be replaced by either oxygen, sulfur, SO_2 , $C=O$, NH , or NCH_3 .

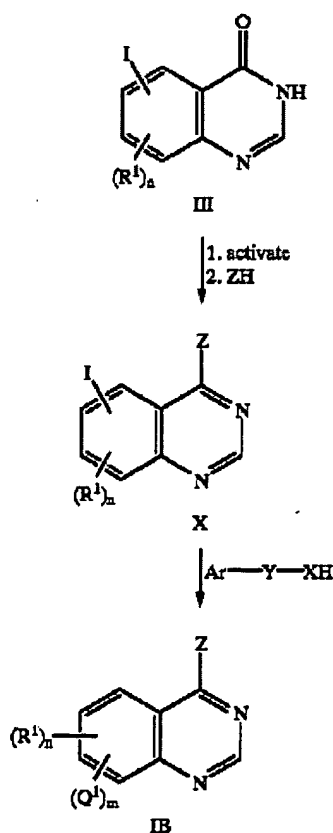
Formula XI differs from the instant formula 3 by having Ar (or a ring) as a terminal group, and not a group corresponding to the claimed $(R^{20})-C(=O)-N-C(=O)-(R^{19})$. However, the difference in the terminal groups of the two formulae does not affect the reaction. As described by Berrée et. al., the groups such as: $(R^{20})-C(=O)$ and $(=O)-(R^{19})$ merely act as nitrogen protecting groups.

The coupling reaction between formulae XI and X is carried out in the presence of a catalyst and a base just as the reaction of formulae 2 and 3 as claimed herein. For instance, on column 21 of US'318, Example 6 describes the reaction carried out in the presence of **palladium**

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acetate (a catalyst recited in the instant claim 17), the base of **triethylamine** (which falls within the group $(R)_3N$ of the instant claim 19), and the solvent of **acetonitrile**. The reaction is also carried out at the temperature of 100°C , which is within the range of $25^{\circ}\text{C} - 175^{\circ}\text{C}$ recited in the instant claim 22.

The ligand (recited in the instant claim 18) is actually involved in the preparation of formula 2 as recited in the instant claim 23. the preparation of formula 2 corresponds to the preparation of the disclosed formula X, which can be found in Scheme 7 on column 3, or see below:

SCHEME 7

(X is C_2 alkene or C_2 alkyne)

Although a formula corresponding to the instant formula 2A is not explicitly disclosed, it would be within the level of the skilled chemist to understand that when the disclosed formula III is activated with a ligand (e.g., **triphenylphosphine**) and a chlorinating agent (e.g., POCl_3), then the oxo group of formula III is converted into a Cl, which would yield a product equivalent to the instant formula 2A (see columns 14-16 for the description of Schemes 1-9 of US'318).

Therefore, at the time that the invention was made, it would have been obvious to develop a process of making compounds of formula 1 in view of the combined teachings of **Sobolov-Jaynes et. al.** and **Berrée et. al.**

The applied reference of 6,225,318 has a common inventor, and is commonly assigned with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

3. Claims 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Berrée et. al.** (Syn. Comm., 29(15), 2685-2693 (1999)—cited on IDS) in view of **March** (Advanced Organic Chemistry..., 1992).

Claim 24 basically recites the process of deprotecting the instant formula 1 by cleaving off either group $R^{20}-C(=O)-$, or $R^{19}-C(=O)-$ to obtain formula 5. Claim 26 basically recites the cleavage of both $R^{20}-C(=O)-$, and $R^{19}-C(=O)-$, and reacting the product (i.e., formula 4) with $ClC(O)(CR^{15}R^{16})_lOR^{17}$ or a reactive equivalent thereof.

On page 2687, in Scheme 5, **Berrée et. al.** generically disclosed a process of converting a tertiary amine to a secondary amine by reacting the tertiary amine with an acid (specifically, **trifluoroacetic acid**, or TFA). Said process would have given sufficient guidance for the skilled chemist to convert formula 1 to formula 5 as recited in the instant claims 24 and 25 (reciting specific products) because formula 1 is a tertiary amine while formula 5 is a secondary amine.

Since the process of claim 29 is essentially like that of claim 24, it is also obvious over the teaching of **Berrée et. al.** for the same reason.

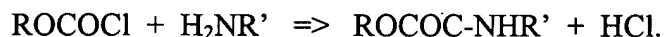
Likewise, it would be within the level of one skilled in the art to further convert a secondary amine to a primary amine using **Berrée's** process. Such a conversion would be applicable in step (a) of the instant claim 26 because formula 4 is a primary amine. Another word, the process of deprotecting the amine from carbamates as recited in the instant claims 24, 29 and step (a) of the instant claim 26 is predictable and well known in the art as acknowledged by **Berrée et. al.**, and revealed by **March**.

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Step (b) of the instant claim 26 is in effect the acylation of a primary amine (i.e., formula 4) with a $\text{ClC(O)(CR}^{18}\text{R}^{19})\text{OR}^{17}$, or a **reactive equivalent thereof** to form a carbamate such as the instant formula 5 (or a secondary amine). On page 418, March states that:

“When chloroformates ROCOCl are treated with primary amines, carbamates are obtained.”

In essence, March teaches the following reaction:



March also teaches the use of a base such as aqueous alkali for combining with the liberated HCl . March also reveals that when the chloroformate is unstable (e.g., Me_3COCOCl), its anhydride is used instead (e.g., $(\text{Me}_3\text{COCO})_2\text{O}$). Such a disclosure renders obvious claims 27 and 28 as well.

Thus, although only generically taught, the processes of **Berrée et. al.** and **March** are predictable and standard in the chemical art for deprotecting and acylating an amine of any structure or size.

Therefore, at the time that the invention was made, it would have been obvious to develop a process as claimed herein in view of the combined teachings above.

No pending claim is allowed.

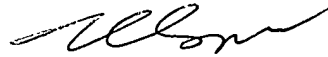
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (9:30-6:00).

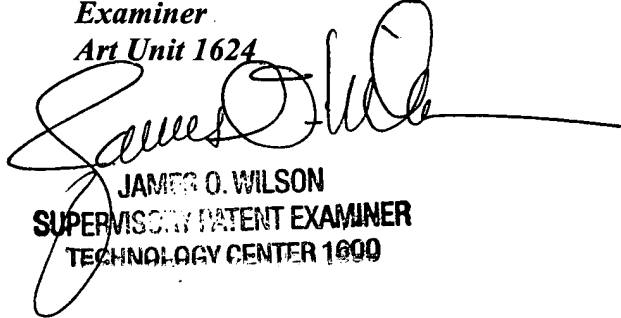
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

8-4-05


Tamthom N. Truong
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Art Unit 1624


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